

Association between particulate air pollution and methylation of transcript variants of mRNA in an elderly cohort: Veterans Administration Normative Aging Study

Marie-Abele Bind, *Harvard School of Public Health, US*

Andrea Baccarelli, *Harvard School of Public Health, US*

Letizia Tarantini, *University of Milan, Italy*

Helen Suh, *Harvard School of Public Health, US*

Pantel Vokonas, *Boston University School of Medicine, US*

Joel Schwartz, *Harvard School of Public Health, US*

Background and Aims: The mechanisms of particle effects are still being elucidated but may include epigenetic changes. We investigated the association between exposure to $PM_{2.5}$ and methylation of transcript variants of mRNA in the elderly, a suspected risk group.

Methods: We examined the relationship between $PM_{2.5}$ and methylation of transcript variants of mRNA in leukocytes in 141 men participating in the NAS study (1999-2007). We selected 1258 transcripts variants of mRNA (out of 24211) that displayed the largest variance across participants. We randomly split our data set in a test set ($n=79$) and a validation set ($n=62$). We investigated the intermediate- (24h-mean, 2, 7, and, 30 days moving average ($MA_{2days}, MA_{7days}, MA_{30days}$)), and long-term (1 year moving average (MA_{1year})) effects of $PM_{2.5}$ adjusting for age, body mass index, smoking, temperature, season, and percentages of neutrophil and lymphocyte in differential blood count.

Results: We found a significant positive association between $PM_{2.5}$ (MA_{7days}) and methylation of ubiquitin-conjugating enzyme E2A ($p_{test}=0.017, p_{validation}=0.009$). This enzyme is required for post-replicative DNA damage repair and plays a role in blood pressure regulation. We observed a significant positive association between $PM_{2.5}$ (MA_{7days}) and methylation of ATP-binding cassette ($p_{test}=0.032, p_{validation}=0.007$).

$PM_{2.5}$ (MA_{30days}) was associated with methylation of dual specificity phosphatase 10 ($p_{test}=0.010, p_{validation}=0.015$).

We found a significant negative association between $PM_{2.5}$ (MA_{1year}) and methylation of microsomal triglyceride transfer protein (MTTP) ($p_{test}=0.035, p_{validation}=0.011$). MTTP is a common genetic variation in multiple metabolic pathways which influences susceptibility to low HDL-cholesterol and coronary heart disease. We observed a significant positive association between $PM_{2.5}$ (MA_{1year}) and methylation of immunoglobulin-like and fibronectin type III domain containing 1 ($p_{test}=0.0008, p_{validation}=0.0313$). We obtained a significant positive association between $PM_{2.5}$ (MA_{1year}) and methylation of cerebellin 1 precursor, a cerebellum-specific protein ($p_{test}=0.005, p_{validation}=0.019$).

Conclusions: Our results suggest an association between intermediate- and long-term exposures to particulate air pollution and methylation transcript variants of mRNA.